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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,955	10/31/2003	Edward A. Neuwelt	720109.404	8802
500	7590	12/21/2005	EXAMINER	
SEED INTELLECTUAL PROPERTY LAW GROUP PLLC			CHOI, FRANK I	
701 FIFTH AVE			ART UNIT	
SUITE 6300			PAPER NUMBER	
SEATTLE, WA 98104-7092			1616	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/698,955

Applicant(s)

NEUWELT ET AL.

Examiner

Frank I. Choi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/15/2004</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5,7,14-22,29 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Neuwelt et al. (Reference CK in PTO-1449 (7/15/2005)).

Neuwelt et al. expressly disclose the amelioration/prevention of decrease in platelets due to carboplatin, etoposide phosphate and melphalan treatment of brain and non-brain cancer, using N-acetylcysteine with or without sodium thiosulfate, post and/or prior to chemotherapy, with or without blood brain barrier disruption (Pgs. 7868-7871)

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being obvious over Neuwelt et al. (Reference CK) in view of Muldoon et al. (Reference CH) and Doolittle et al. (Blood (November 2001)).

Neuwelt et al. discloses the amelioration/prevention of decrease in platelets due to carboplatin, etoposide phosphate and melphalan treatment of brain and non-brain cancer, using

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N-acetylcysteine with or without sodium thiosulfate, post and/or prior to chemotherapy, with or without blood brain barrier disruption (Pgs. 7868-7871). It is disclosed that after osmotic blood brain barrier disruption (BBBD), sodium thiosulfate administration must be delayed at least 60 minutes when the blood brain barrier is reestablished or seizures result (Pg. 7872). It is disclosed that recent data suggests that delayed sodium thiosulfate may provide platelet protection in brain tumor patients (Pg. 7871).

Muldoon et al. discloses that sodium thiosulfate, N-acetylcysteine and glutathione ethyl ester act as chemoprotectants against toxicity of carboplatin, cisplatin, etoposide phosphate and melphalan, with maximally effective protection against melphalan toxicity occurring if administered concurrently, whereas chemoprotection for the platinum agents remained effective if delayed at least 4 hours (Pgs. 797-803). It is disclosed that chemoprotection with sodium thiosulfate did not reduce the efficacy of carboplatin if administration was delayed for 8 hours after chemotherapy (Pg. 804). It is disclosed that sodium thiosulfate may be safely administered in single bolus doses up to 20 g/m² (Pg. 803).

Doolittle et al. discloses that delayed administration of 16-20 gm/m², based on blood/bone marrow toxicity data, may protect against severe thrombocytopenia in patients treated with a carboplatin-based BBBD regimen in which cyclophosphamide, etoposide or etoposide phosphate, and G-CSF were part of the regimen (Abstract).

The difference between the prior art and the claimed invention is that the prior art does not explicitly disclose a method of ameliorating/preventing thrombocytopenia induced by chemotherapy where the administration of the active agent is concurrent, delayed for at least 30 minutes, or used to treatment in humans. However, the prior art amply suggests the same

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treatment of animals with N-acetylcysteine or sodium thiosulfate has been effective in protecting platelets from chemotherapy toxicity, including pre and post administration, sodium thiosulfate should be administered at least 60 minutes after BBBD. As such, it would have been well within the skill of and one of ordinary skill in the art would have expected that concurrent administration would also be effective, that administration at least 30 minutes or more would also be effective and that disclosed methods would also be effective in ameliorating/preventing decrease in platelets in humans.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

FIC

December 9, 2005

JOHN PAK
PRIMARY EXAMINER
GROUP 1600